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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,938	03/19/2004	John Link	10031165-1	8132

7590 12/04/2007

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
12/04/2007	PAPER

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/804,938
Filing Date: March 19, 2004
Appellant(s): LINK ET AL.

Bret E. Field
For Appellant

EXAMINER'S ANSWER

This is in response to the Appeal Brief filed 14 September 2007 appealing from the Office Action mailed 26 March 2007 and 26 June 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. Applicant's After Final amendments filed 25 May 2007 have overcome the rejection of claims 3-6 as being indefinite under 35 U.S.C. 112, second paragraph. The rejections are therefore withdrawn.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Sambrook et al, "Molecular Cloning, A Laboratory Manual" 2nd Edition, Cold spring Harbor Laboratory Press, NY (1989), pp. 7.12-7.15 and 7.23-7.29

Pall Life Sciences Bulletin #FAM-1050-C, Pall Corporation, Filterite Advanced Materials Division, San Diego, CA (2002)

5,219,727	Wang et al	6-1993
5,906,742	Wang et al	5-1999
5,627,027	Waggoner	5-1997

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

Claims 1, 3-6, 10-15, and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993) in view of Wang et al (U.S. Patent No. 5,906,742, issued 25 May 1999) as evidenced by Pall Life Sciences (Bulletin #FAM-1050-C, Pall Corporation, Filterite Advanced Materials Division, San Diego, CA, 2002).

Regarding claims 1, 3-4, 10-15, and 20-21, Sambrook et al teach a method of preparing an RNA sample substantially free of contaminants. In a single exemplary embodiment, Sambrook et al teach preparation of an RNA sample (pages 7.23), followed by addition of the organic solvent ethanol (i.e., claim 14) to the RNA sample (page 7.25, step 19). Sambrook et al further teach the RNA preparation is subjected to removal of DNA by the enzyme DNAse I (i.e., claim 20), which is added to the RNA sample

preparation ("note" on page 7.25, and page 7.14, steps 10-17). Sambrook et al further teach addition of a wash buffer (i.e., solution) comprising the chaotropic agent guanidine hydrochloride (i.e., claim 21; page 7.24, step 6). Sambrook et al further teach contacting an RNA isolation membrane column with said RNA-containing precipitate; namely, performing chromatography on the RNA (page 7.15, paragraph ii). The chromatography is performed in a column comprising a membrane; namely, a Pasteur pipette comprising a oligo(dT) cellulose and a glass wool plug (page 7.26, step 2). The glass wool of Sambrook et al is interpreted as a membrane because a "wool" comprises a multi-fiber interwoven structure (i.e., a membrane) having spaces between individual fibers (i.e., pores). Because the column has oligo(dT) cellulose, the column is an RNA isolation column because polyadenlyated (i.e., polyA+) RNAs are isolated by the column (i.e., claim 15). The RNA is then eluted from the membrane column (page 7.29).

Claims 10-13 are drawn to RNA that is from about 55-65, 65-75, 75-85, and 85 to $\geq$95% pure. The claims do not define what the RNA is purified from so as to define the purity. Because Sambrook et al teach the RNA is separated and purified (page 7.15, paragraph ii), the RNA of Sambrook et al is encompassed by the broadly claimed purity of instant claims 10-13.

It is noted that the claim appears to be drawn to a method wherein both the addition of the DNAse enzymes and the addition of the chaotropic salt occur while the RNA sample is still on the column. While Sambrook et al does not explicitly teach the DNAse and the chaotropic salt are added to the RNA on the column, the courts have held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946)). See MPEP 2144.04 IV.C.

Sambrook et al do not teach the RNA is cRNA.

However, Wang et al teach a method of preparing a cRNA sample substantially free of contaminants using an RNA isolation column in the form of selective elution of cRNA from a QIAGEN-tip spin column and oligo(dT) chromatography (column 13, Example 1). Wang et al further teach that a

single cRNA has the added advantage of allowing quantitation of mRNA as well as acting as a internal standard template for reverse transcription reactions (column 8, line 65-column 9, line 23).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of preparing an RNA sample substantially free of contaminants as taught by Sambrook et al to prepare cRNA as taught by Wang et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method of preparing a cRNA sample substantially free of contaminants and having the added advantage of purifying an RNA which can be used for quantitation of mRNA as well as acting as a internal standard template for reverse transcription reactions as explicitly taught by Wang et al (column 8, line 65-column 9, line 23).

Regarding claims 3-4, the Specification teaches that MMM membranes are available from Pall Life Sciences (page 15, paragraph 0061). Bulletin #FAM-1050-C from Pall Life Sciences defines MMM membranes as asymmetric membranes composed of polysulfone and PVP.

While Sambrook et al teach the column comprises a membrane (column 6, lines 52-55), Sambrook et al and Wang et al are silent with respect to MMM membranes (i.e., claims 3-4).

However, Wang et al '742 teach the use of solid phases in the form of asymmetric microfiltration membrane materials (Abstract, lines 1-2) comprising PVP (i.e., polyvinylpyrrolidone) co-cast with polysulfone (Abstract, lines 7-11) for filtering biological samples (e.g., whole blood; Abstract, lines 11-12) with the added advantage that the membranes are highly useful in the quick detection of components contained in liquid samples (Abstract, lines 14-16).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising a membrane as taught by Sambrook et al and Wang et al with the membrane as taught by Wang et al '742 with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because such a modification would have resulted in a method of preparing a cRNA sample substantially

free of contaminants having the added advantage of allowing the quick detection of components contained in liquid samples as explicitly taught by Wang et al (Abstract, lines 14-16).

Regarding claims 5-6, the method of claim 3 is discussed above. Wang et al '742 also teach the MMM membrane has a pore size ranging from about 30 μm to about 40 μm on an upper side, and wherein said MMM membrane has a pore size of about 0.8 μm on a lower side; namely, the membrane of Wang et al '742 has a pore size around 1.0 μm (which is the "about 0.8μm" of the claim) and opens to about 50 μm (which is the "about 40 μm" of the claim; column 10, line 59- column 11, line 1). In addition, the courts have stated where the claimed ranges "overlap or lie inside the ranged disclosed by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP 2144.05.01). Therefore, the claimed range of a pore size ranging from about 30 μm to about 40 μm on an upper side, and wherein said MMM membrane has a pore size of about 0.8 μm on a lower side would have been obvious under the pore size around 1.0 μm that opens to about 50 μm as taught by Wang et al '742.

It is noted that the rejections of claims 1, 3-6, 10-15, and 20-21 are not new rejections. Claims 1, 10-15, and 21 were previously rejected under 35 USC 103(a) in the Final Office Action mailed 26 March 2007 as obvious over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993). Claims 2-6 were also previously rejected under 35 USC 103(a) in the Final Office Action mailed 26 March 2007 as obvious over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993) as applied to the previous version of claim 1, and further in view of Wang et al (U.S. Patent No. 5,906,742, issued 25 May 1999) as evidenced by Pall

Life Sciences (Bulletin #FAM-1050-C, Pall Corporation, Filterite Advanced Materials Division, San Diego, CA, 2002). However, as noted in the Advisory Action mailed 26 June 2007, the entering of the after final amendments to independent claim 1 would result in rejection of claims 1, 3-6, 10-15, and 20-21 under 35 USC 103(a) for the reasons set forth in the rejection of claim 2 (now cancelled as a result of entering the after final amendments of 25 May 2007). Thus, the rejections of claims 1, 3-6, 10-15, and 20-21 under 35 USC 103(a) are not new rejections, but are rejections of record reiterated above.

Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993) in view of Wang et al (U.S. Patent No. 5,906,742, issued 25 May 1999) as evidenced by Pall Life Sciences (Bulletin #FAM-1050-C, Pall Corporation, Filterite Advanced Materials Division, San Diego, CA, 2002).) as applied to claim 1 above, and further in view of Waggoner (U.S. Patent No. 5,627,027, issued 6 May 1997).

Regarding claims 7-9, the method of claim 1 is discussed on pages 3-6 above. While Wang teaches labeled amplified DNA (column 11, lines 59-67), neither Sambrook et al, Wang et al, nor Wang '742 teach labeled RNA.

However, Waggoner teaches the labeling of RNA using fluorescent cyanine dyes (i.e., claims 8-9; Abstract) with the added advantage that cyanine-labeled nucleic acids help reduce non-specific binding to irrelevant components in a mixture (Abstract, last five lines).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Sambrook et al in view of Wang et al and Wang '742 with the label as taught by Waggoner with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because such a modification would have resulted in a method of preparing a cRNA sample substantially free of contaminants having

the added advantage of reduction of non-specific binding to irrelevant components in a mixture as explicitly taught by Waggoner (Abstract, last five lines).

It is noted that the rejections of claims 7-9 of are not new rejections. Claims 7-9 were previously rejected under 35 USC 103(a) in the Final Office Action mailed 26 March 2007 as obvious over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993) as applied to claim 1, and further in view of Waggoner (U.S. Patent No. 5,627,027, issued 6 May 1997). However, as noted in the Advisory Action mailed 26 June 2007, the entering of the after final amendments to independent claim 1 would result in rejection of claims 7-9 under 35 USC 103(a) for the reasons set forth in the rejection of claim 2 (now cancelled as a result of entering the after final amendments of 25 May 2007). Thus, the rejections of claims 7-9 under 35 USC 103(a) are not new rejections, but are rejections of record reiterated above.

(10) Response to Argument

Appellant states on pages 6-7 of the Appeal Brief filed 14 September 2007 (i.e., the "Brief") that the claims will be argued in groups as follows:

Group I, claims 1, 3-4, 7-9, 14-15, and 20-21;

Group II, claim 5;

Group III, claim 6;

Group IV, claim 10;

Group V, claim 11;

Group VI, claim 12; and

Group VII, claim 13.

The examiner's response to Appellant's argument based on the order of Groups I-VII as presented by Appellant in the Brief.

Appellant's arguments on pages 7-8 of the Brief regarding the rejections under 35 U.S.C. 112, second paragraph have been considered but are moot in view of the withdrawn rejections.

Group I: Claims 1, 3-4, 7-9, 14-15, and 20-21

Appellant argues on pages 8-10 of the Brief that the combined teachings of Sambrook et al, Wang et al, and Wang et al '742 do not teach a cRNA isolation column that does not have an active binding agent associated therewith.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a column that does not have an active binding agent associated therewith) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Appellant further argues on page 10 of the Brief that the closed claim language of claim 1 excludes membranes that have an active binding agent associated therewith.

However, claim 1 specifically recites "said cRNA isolation column **comprises** a membrane **selected from the group** consisting of polysulfone treated with hydroxypropylcellulose, PVDF (polyvinylidene fluoride), nylon, nitrocellulose, polysulfone and polyvinylpyrrolidone, polyvinylpyrrolidone (PVP), and composites thereof. " (emphasis added by examiner) Thus, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents. As noted in the rejections presented above in Section (9) above, Sambrook et al teach RNA chromatography is performed in a Pasteur pipette comprising a membrane in the form of a glass wool plug **and** oligo(dT) cellulose (page 7.26, step 2). The column therefore comprises a membrane in the form of a glass wool plug.

Appellant also argues on page 1 of the Remarks that the glass wool of Sambrook et al is not a membrane because, because "the membrane material plays a passive role, acting as a physical barrier to the precipitate" as stated on page 19, line 23 to page 20, line 6 of the instant specification.

Sambrook et al explicitly state in step 2 of page 7.26 that the column is "plugged" with sterile glass wool. The "plugging" of the column thus prevents passage of the oligo-(dT)-cellulose and also prevents passage of any precipitates precisely by acting as a physical barrier; i.e., as a plug. Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "membrane" (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]). Any additional retention of materials by specific binding agents in the column prior to contact with the membrane is encompassed by the open claim language "comprising" of the instant claim.

In addition, with respect to membranes, it is noted that Sambrook is not relied upon for the specific membrane of the instant claim; rather, Sambrook et al is relied upon for a column comprising a membrane, and Wang et al '742 is relied upon for a functionally equivalent membrane in the form of an asymmetric microfiltration membrane. Thus, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Appellant asserts on page 12 of the Brief that neither Wang et al nor Wang et al '742 cures the deficiencies of Sambrook et al with regard to the membranes.

However, as noted above in Section (9), the Specification teaches that MMM membranes, which are an embodiment of the claimed membrane, are available from Pall Life Sciences (page 15, paragraph 0061). Bulletin #FAM-1050-C from Pall Life Sciences defines MMM membranes as asymmetric membranes composed of polysulfone and PVP.

Wang et al '742 teach the use of solid phases in the form of asymmetric microfiltration membrane materials (Abstract, lines 1-2) comprising PVP (i.e., polyvinylpyrrolidone) co-cast with polysulfone (Abstract, lines 7-11) for filtering biological samples (e.g., whole blood; Abstract, lines 11-12) with the added advantage that the membranes are highly useful in the quick detection of components contained in liquid samples (Abstract, lines 14-16).

The examiner therefore maintains that the combination of references does, in fact, make obvious the claimed invention for the reasons reiterated herein; namely, the ordinary artisan would have been motivated to make such a modification because such a modification would have resulted in a method of preparing a cRNA sample substantially free of contaminants having the added advantage of allowing the quick detection of components contained in liquid samples as explicitly taught by Wang et al (Abstract, lines 14-16).

In addition, Wang et al '742 clearly teach the known technique of using mixed PVP/polysulfone membranes in the filtration of biological samples. The examiner therefore argues that the combination of references does, in fact, make obvious the claimed invention because the known technique of using the membrane of Wang et al '742 could have been applied to the method of Sambrook et al in view of Wang et al with predictable results because the membrane of Wang et al '742 predictably results in a membrane suitable for use in filtration of biological materials.

Appellant further asserts on page 13 of the Brief that the substitution of the membrane of Wang et al '742 for the membrane of Sambrook et al results in a column having an active binding agent associated therewith.

However, as noted above, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents.

Appellant also asserts on page 13 of the Brief that the combination of Sambrook et al, Wang et al, and Wang et al '742 does not teach a membrane which passively retains an RNA precipitate.

However, the claims do not recite an RNA precipitate; rather, the claims recite "an organic preparation" in step (c), "a preparation" in steps (d) and (e), and "eluting said cRNA" in step (f). The word "precipitate" is not used in any of the claims. Thus, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., retention of an RNA precipitate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Appellant argues on pages 13-14 of the Brief that the examiner's citation of *In Re Kerkhoven* is inapplicable because the instant rejections do not combine two compositions.

Applicant's assertion is correct because the rejection does not combine two compositions to form a third composition. However, the argument is moot because Wang et al '742 provide a teaching, suggestion and motivation to use the asymmetric membranes because the membranes have the added advantage of being highly useful in the quick detection of components contained in liquid samples (Abstract, lines 14-16). Wang et al '742 also clearly teach the known technique of using mixed PVP/polysulfone membranes in the filtration of biological samples.

The examiner therefore maintains that the combination of references does, in fact, make obvious the claimed invention for the reasons reiterated herein; namely; the ordinary artisan would have been motivated to make such a modification because such a modification would have resulted in a method of preparing a cRNA sample substantially free of contaminants having the added advantage of allowing the quick detection of components contained in liquid samples as explicitly taught by Wang et al (Abstract, lines 14-16). In addition, it would also have been obvious to the ordinary artisan that the known technique of using the membrane of Wang et al '742 could have been applied to the method of Sambrook et al in view of Wang et al with predictable results because the membrane of Wang et al '742 predictably results in a membrane suitable for use in filtration of biological materials.

Group II: Claim 5

Appellant asserts on pages 14-16 of the Brief that because Wang et al '742 teach membranes having pore sizes around 1.0 micron (i.e., μm) followed by an asymmetric region that opens from pore sizes of approximately 2 microns to 50 microns, Wang et al '742 does not teach a membrane ranging from about 30 to about 50 microns on an upper side and a pore size from about 0.4 microns to about 0.6 microns on a lower side because the about 0.4 microns to about 0.6 microns of the instant claim is approximately half the size of the about 1 micron of the membrane of Wang et al '742.

However, a review of the specification yields no limiting definition of the range of variance encompassed by the term "about." Thus, as noted above in Section (9), the instantly claimed "about 0.6 microns" is an obvious variant of the "approximately 1.0 micron" of Wang et al '742.

Appellant further asserts on page 16 of the Brief that Appellants have demonstrated unexpected results for cRNA purification conducted using a membrane with the claimed pore size ranges, as shown in Figure 14 in the instant specification.

However, the method of purification used to produce the results cited in Figure 14 is not commensurate in scope with the method of instant claim 5. Example 12 of the instant specification, which describes the protocol used to obtain the results of Figure 14, differs from the method of claim 5 by at least the following:

A. Example 12 states that the cRNA is isolated using Agilent Technologies' Low RNA Input Fluorescent Linear Amplification kit, as described in version 1.1, pages 9-13 (hereafter "the Agilent reference"). Page 9 of the Agilent reference specifically requires "high quality total or poly-A+ RNA." This instant claim does not require such high quality starting material.

B. Page 10, step 3 and the CDNA master mix; page 11, Transcription Master Mix; and page 13, steps 16 and 23, all require the use of RNAse free water for elution of the cRNA. RNAses degrade RNAs, including cRNAs. **Thus, the specific exclusion of RNAses from the elution**

solution would inherently increase the yield of RNA generated by the protocol of Example 12. RNAse free water is not required by the instant claim.

C. Example 12 requires the addition of 250 microliters (i.e., μL) of Stabilization Solution prior to contacting the column. The Stabilization Solution comprises 4 M Guanidine Thiocyanate, 25 mM Tris, pH 7, and 143 mM β-mercaptoethanol (page 24 of the specification). None of these agents are required by the instant claim, but are required for Figure 14.

D. Example 12 further requires centrifugation of the sample through the column. The instant claim does not require centrifugation.

E. Claim 1, upon which claim 5 depends, requires one or more DNAse enzymes. No DNAse enzymes are used in Example 12.

F. Example 12 also requires Wash buffer #3, which comprises 5 to 250 mM Tris, pH form about 6 to about 9, and from about 40 to about 90% ethanol (page 24 of the specification). None of these agents are required by the instant claim, but are required for Figure 14.

G. Example 12 requires an additional centrifugation step after washing of the sample on the column. The instant claim does not require any centrifugation.

H. Example 12 specifically requires the use of RNAse free water for elution of the cRNA. RNAses degrade RNAs, including cRNAs. **Thus, the specific exclusion of RNAses from the elution solution would inherently increase the yield of RNA generated by the protocol of Example 12. RNAse free water is not required by the instant claim.**

I. Example 12 further requires yet another centrifugation step, as well as repetition of the RNAse free water elution and final centrifugation step after washing of the sample on the column. The instant claim does not require any centrifugation or RNAse free water.

Thus, it is unclear if the results presented in Figure 14 and Example 12 of the instant specification are unexpected results because the results relied upon are produced by a method that is not commensurate in scope with the instant claims.

In addition, in citing Figure 14 of the instant specification, Applicant argues that the MMM membranes of claim 5, which encompass the instantly claimed pore size of about 0.4 microns, show unexpected results. However, the last column of Figure 14 shows results for a known alternative purification method using silica based spin columns. Applicant's own results using the silica based spin columns presented in Figure 14 are actually slightly better than Applicant's results using the instantly claim 0.4 micron membranes. Thus, the results obtained by Applicant with the instantly claimed "about 0.4 micron" membranes are not unexpected because they do not show better results when compared with Applicant's results with the silica based spin columns of Figure 14.

Group III: Claim 6

Appellant argues on page 17 of the Brief that the substitution of the membrane of Wang et al '742 for the membrane of Sambrook et al results in a column having an active binding agent associated therewith.

However, as noted above, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents.

Appellant also argues on page 17 of the Brief that the combination of Sambrook et al, Wang et al, and Wang et al '742 does not teach a membrane which passively retains an RNA precipitate.

However, the claims do not recite an RNA precipitate; rather, the claims recite "an organic preparation" in step (c), "a preparation" in steps (d) and (e), and "eluting said cRNA" in step (f). The word "precipitate" is not used in any of the claims. Thus, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which

applicant relies (i.e., retention of an RNA precipitate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Appellant further argues on page 17 of the Brief that because Wang et al '742 teach membrane having pore sizes around 1.0 micron (i.e., μm) followed by an asymmetric region that opens from pore sizes of approximately 2 microns to 50 microns, Wang et al '742 does not teach a membrane ranging from about 30 to about 50 microns on an upper side and a pore size to about 0.4 microns on a lower side because the about 0.4 microns of the instant claim is approximately half the size of the about 1 micron of the membrane of Wang et al '742.

However, a review of the specification yields no limiting definition of the range of variance encompassed by the term "about." Thus, as noted above in Section (9), the instantly claimed "about 0.4 microns" is an obvious variant of the "approximately 1.0 micron" of Wang et al '742.

Group IV: Claim 10

Appellant asserts on pages 17-18 of the Brief that the substitution of the membrane of Wang et al '742 for the membrane of Sambrook et al results in a column having an active binding agent associated therewith.

However, as noted above, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents.

Appellant also asserts on page 18 of the Brief that the combination of Sambrook et al, Wang et al, and Wang et al '742 does not teach a membrane which passively retains an RNA precipitate.

However, the claims do not recite an RNA precipitate; rather, the claims recite "an organic preparation" in step (c), "a preparation" in steps (d) and (e), and "eluting said cRNA" in step (f). The word "precipitate" is not used in any of the claims. Thus, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which

applicant relies (i.e., retention of an RNA precipitate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Appellant further asserts on pages 18-19 of the Brief that because Sambrook et al teach oligo-(dT)-cellulose produces RNA that is "approximately equal" in poly A+ RNA and non-poly A RNA (i.e., approximately 50% poly A+ RNA and 50% non-poly A RNA) the purified RNA is not from about 55% to about 65% pure.

However, a review of the specification yields no limiting definition of the range of variance encompassed by the term "about." Thus, the "approximately equal" (i.e., "approximately" 50%) purity of Sambrook et al is encompassed by the "about 55%" of the instant claim.

In addition, as noted above in Section (9), the claims do not define what the RNA is purified from so as to define the purity. For example, Sambrook et al teach RNA is purified using an elution buffer containing Tris, EDTA, and SDS (step 7, page 7.27), followed by centrifugation, washing, and resuspension in ethanol (page 7.28-7.29). These steps remove the Tris, EDTA, and SDS; thus, the purity of the RNA sample is measurable against the residual amount of Tris, EDTA, and SDS. The purity is therefore high because most of the Tris, EDTA, and SDS is removed by the recited steps. Because the purity of the RNA sample is readily related to numerous alternative parameters (i.e., starting purity, purity between two steps of the method, etc), the purity of the RNA of Sambrook et al is encompassed by the broadly claimed purity of instant claims 10-13.

Group V: Claim 11

Appellant argues on page 19 of the Brief that the substitution of the membrane of Wang et al '742 for the membrane of Sambrook et al results in a column having an active binding agent associated therewith.

However, as noted above, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents.

Appellant also argues on page 19 of the Brief that the combination of Sambrook et al, Wang et al, and Wang et al '742 does not teach a membrane which passively retains an RNA precipitate.

However, the claims do not recite an RNA precipitate; rather, the claims recite "an organic preparation" in step (c), "a preparation" in steps (d) and (e), and "eluting said cRNA" in step (f). The word "precipitate" is not used in any of the claims. Thus, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., retention of an RNA precipitate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Appellant further argues on pages 19-20 of the Brief that because Sambrook et al teach oligo-(dT)-cellulose produces RNA that is "approximately equal" in poly A+ RNA and non-poly A RNA (i.e., approximately 50% poly A+ RNA and 50% non-poly A RNA) the purified RNA is not from about 55% to about 65% pure.

However, as noted above, a review of the specification yields no limiting definition of the range of variance encompassed by the term "about." Thus, the "approximately equal" (i.e., "approximately" 50%) purity of Sambrook et al is encompassed by the "about 65%" of the instant claim.

In addition, it is noted that a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005)(reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component); Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361,

47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed."). Thus, the teaching of Sambrook et al that the purified RNA **usually** contains approximately equal quantities polyA+ and non-poly A+ RNA also encompasses the alternate teaching wherein the poly-A+ RNA **does not** contains equal quantities polyA+ and non-poly A+ RNA, and has greater than 50% purity, which is encompassed by the term "about 65%." See MPEP § 2123 [R-5].

In addition, as noted above for claim 10, because the purity of the RNA sample is readily related to numerous alternative parameters (i.e., starting purity, purity between two steps of the method, etc), the purity of the RNA of Sambrook et al is encompassed by the broadly claimed purity of instant claims 10-13.

Furthermore, on page 18 of the Brief, Appellant cites the last paragraph of page 7.27 of Sambrook et al, which states in part that "to purify poly (a)+ RNA further...carry out a second round of chromatography on the same column of oligo(dT)-cellulose." Thus, Appellant has cited a passage of Sambrook et al indicating that purity of greater than 50% is achieved using the steps of Sambrook et al. An approximately 50% pure sample, as argued by Appellant, when subjected to the second round of chromatography as taught by Sambrook, would necessarily become enriched by at least some increase above "approximately 50%," which is interpreted as the "about 65% to about 75%" of the instant claim.

Group VI: Claim 12

Appellant argues on page 20 of the Brief that the substitution of the membrane of Wang et al '742 for the membrane of Sambrook et al results in a column having an active binding agent associated therewith.

However, as noted above, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents.

Appellant also argues on page 20 of the Brief that the combination of Sambrook et al, Wang et al, and Wang et al '742 does not teach a membrane which passively retains an RNA precipitate.

However, the claims do not recite an RNA precipitate; rather, the claims recite "an organic preparation" in step (c), "a preparation" in steps (d) and (e), and "eluting said cRNA" in step (f). The word "precipitate" is not used in any of the claims. Thus, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., retention of an RNA precipitate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Appellant further argues on pages 20-21 of the Brief that because Sambrook et al teach oligo-(dT)-cellulose produces RNA that is approximately equal in poly A+ RNA and non-poly A RNA (i.e., approximately 50% poly A+ RNA and 50% non-poly A RNA) the purified RNA is not from about 75% to about 85% pure.

However, as noted above, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Thus, the teaching of Sambrook et al that the purified RNA **usually** contains equal quantities polyA+ and non-poly A+ RNA also encompasses the alternate teaching wherein the poly-A+ RNA **does not** contains equal quantities polyA+ and non-poly A+ RNA, and has greater than about 50% purity, which is encompassed by the term "about 75% to about 85% pure."

In addition, as noted above for claim 10, because the purity of the RNA sample is readily related to numerous alternative parameters (i.e., starting purity, purity between two steps of the method, etc), the

purity of the RNA of Sambrook et al is encompassed by the broadly claimed purity of instant claims 10-13.

Furthermore, on page 18 of the Brief, Appellant cites page 7.27, last paragraph of Sambrook et al, which states in part that "to purify poly (a)+ RNA further...carry out a second round of chromatography on the same column of oligo(dT)-cellulose." Thus, Appellant has cited a passage of Sambrook et al indicating that purity of greater than 50% is achieved using the steps of Sambrook et al.
An approximately 50% pure sample as argued by Appellant, when subjected to the second round of chromatography, necessarily becomes enriched by an increase above "approximately 50%," which is interpreted as the "about 75% to about 85%" of the instant claim.

Group VII: Claim 13

Appellant argues on page 21 of the Brief that the substitution of the membrane of Wang et al '742 for the membrane of Sambrook et al results in a column having an active binding agent associated therewith.

However, as noted above, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents.

Appellant also argues on page 21 of the Brief that the combination of Sambrook et al, Wang et al, and Wang et al '742 does not teach a membrane which passively retains an RNA precipitate.

However, the claims do not recite an RNA precipitate; rather, the claims recite "an organic preparation" in step (c), "a preparation" in steps (d) and (e), and "eluting said cRNA" in step (f). The word "precipitate" is not used in any of the claims. Thus, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., retention of an RNA precipitate) are not recited in the rejected claim(s). Although

the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Appellant further argues on pages 21-22 of the Brief that because Sambrook et al teach oligo-(dT)-cellulose produces RNA that is "approximately equal" in poly A+ RNA and non-poly A RNA (i.e., approximately 50% poly A+ RNA and 50% non-poly A RNA) the purified RNA is not from about 75% to about 85% pure.

However, as noted above, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Thus, the teaching of Sambrook et al that the purified RNA **usually** contains equal quantities polyA+ and non-poly A+ RNA also encompasses the alternate teaching wherein the poly-A+ RNA **does not** contains equal quantities polyA+ and non-poly A+ RNA, and has greater than about 50% purity, which is encompassed by the term "about 85%" pure.

In addition, as noted above for claim 10, because the purity of the RNA sample is readily related to numerous alternative parameters (i.e., starting purity, purity between two steps of the method, etc), the RNA of Sambrook et al is encompassed by the broadly claimed purity of instant claims 10-13.

Furthermore, on page 18 of the Brief, Appellant cites page 7.27, last paragraph of Sambrook et al, which states in part that "to purify poly (a)+ RNA further...carry out a second round of chromatography on the same column of oligo(dT)-cellulose." Thus, Appellant has cited a passage of Sambrook et al indicating that purity of greater than 50% is achieved using the steps of Sambrook et al.
An approximately 50% pure sample as argued by Appellant, when subjected to the second round of chromatography, necessarily becomes enriched by an increase above "approximately 50%," which is interpreted as the "about 85%" of the instant claim.

Appellant states on page 22-7 of the Brief that the claims 7-9 will be argued collectively as "Group 1."

Appellant argues on page 22 of the Brief that the substitution of the membrane of Wang et al '742 for the membrane of Sambrook et al results in a column having an active binding agent associated therewith.

However, as noted above, while the membrane is limited to one of the materials of the cited group, the open claim language found in the phrase "said cRNA isolation column comprises a membrane" encompasses any additional material in the column, including active binding agents.

Appellant also argues on page 22 of the Brief that the combination of Sambrook et al, Wang et al, and Wang et al '742 does not teach a membrane which passively retains an RNA precipitate.

However, the claims do not recite an RNA precipitate; rather, the claims recite "an organic preparation" in step (c), "a preparation" in steps (d) and (e), and "eluting said cRNA" in step (f). The word "precipitate" is not used in any of the claims. Thus, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., retention of an RNA precipitate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Appellant's remaining arguments regarding Group 1 rely on arguments regarding set forth to address the rejections of the claims as obvious over Sambrook et al in view of Wang et al in view of Wang et al '742 under 35 U.S.C. 103(a). These arguments are addressed above. Since the arguments regarding the teachings of Sambrook et al in view of Wang et al in view of Wang et al '742 are not persuasive for the reasons set forth above, the remaining rejections of the claims are maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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